

# *Cytogenetics in Hematological Neoplasms*

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## *Some Basic Definitions*

- **Cytogenetics:** Study of chromosomes and the related diseases caused by abnormal chromosome number and / or structure
- **Chromosomes:** Complex structures located in the cell nucleus, composed of DNA, histone and non-histone proteins etc
- **Genes:** The DNA in an individual chromosome is a highly coiled and condensed molecule. Gene is a long segment of DNA coding for a single trait e.g. manufacturing a single protein or enzyme needed for the structure or function of cells. Each Chromosome contains a few thousand genes.



# *Cell Cycle and Metaphase*

- During Interphase, Chromosome are somewhat less condensed and are not visible by light microscope
- During Mitosis or cell division, Chromosomes become highly condensed and can best be identified at the Metaphase stage.
- In Hematological neoplasms we arrest the already dividing cells in Metaphase by using spindle poison e.g. Colchicine

# *Cytogenetics in Hematological Neoplasms*

*Diagnosis of Hematopoietic Neoplasms requires correlation of:*

*Clinical*

*Morphologic*

*Immunophenotypic*

*Molecular/ Cytogenetic Data*

# *Cytogenetics in Hematological Neoplasms*

*Diagnostic Value*

*Prognostic Value*

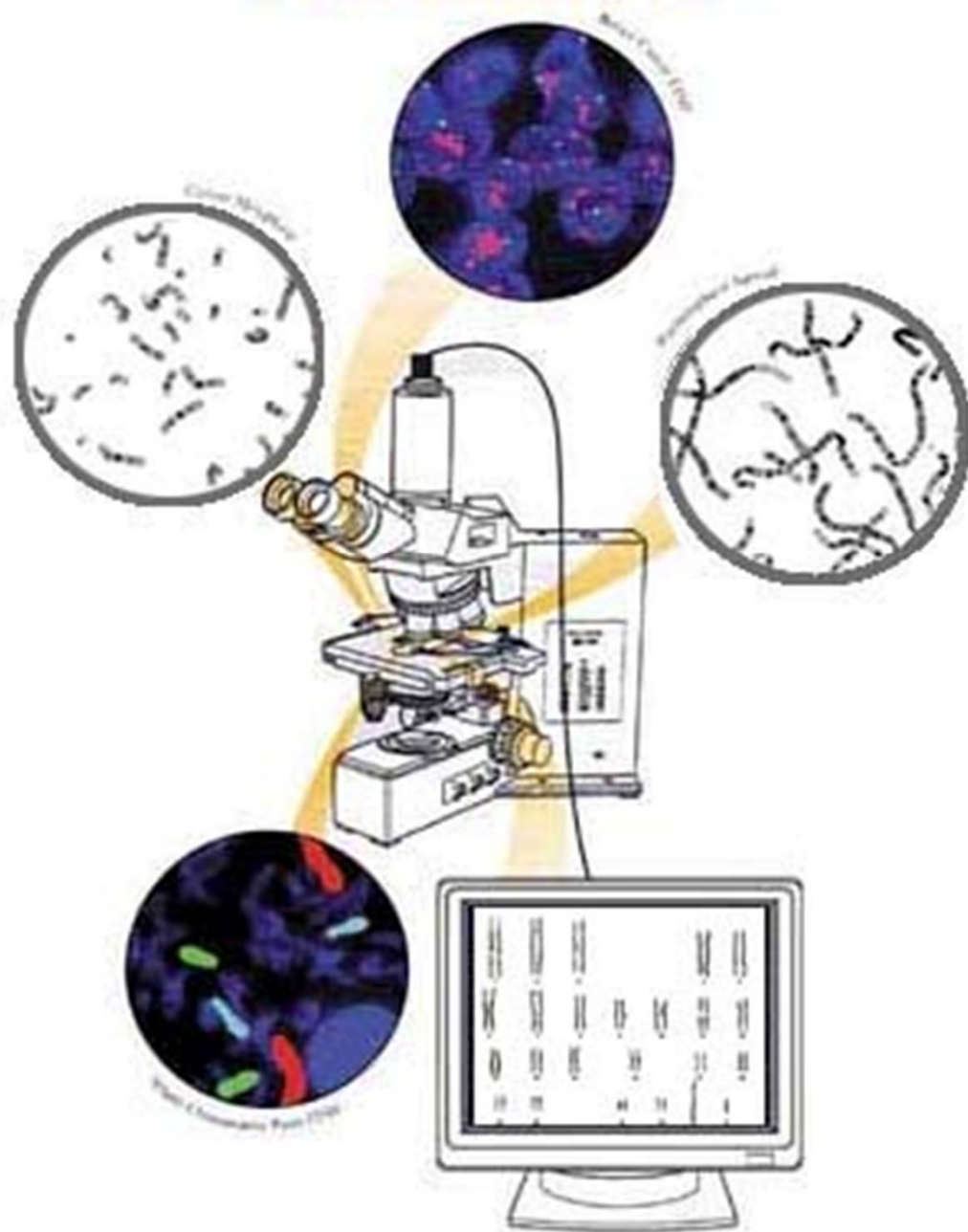
*Treatment Monitoring and MRD*

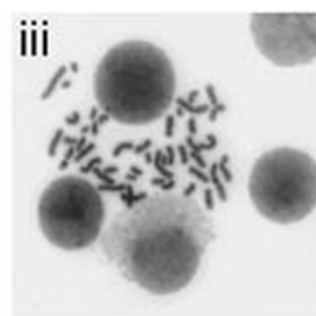
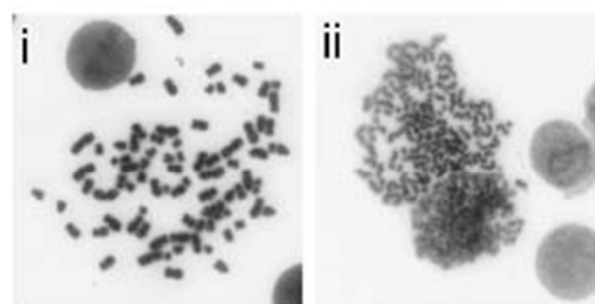
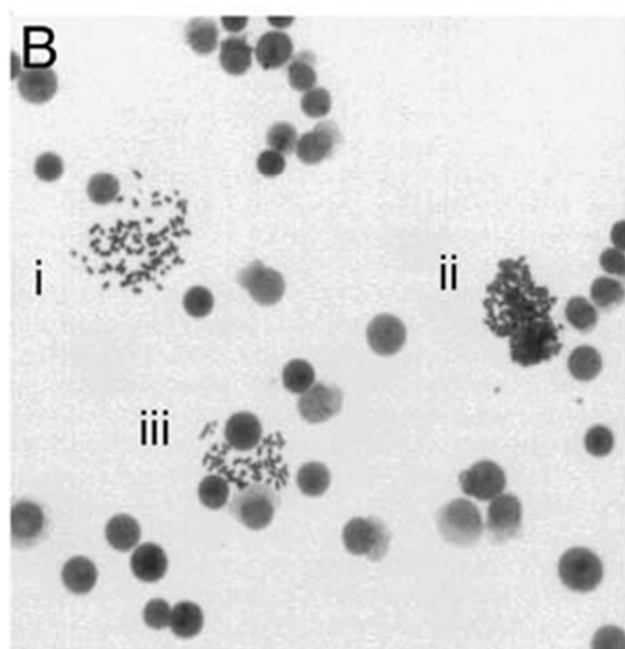
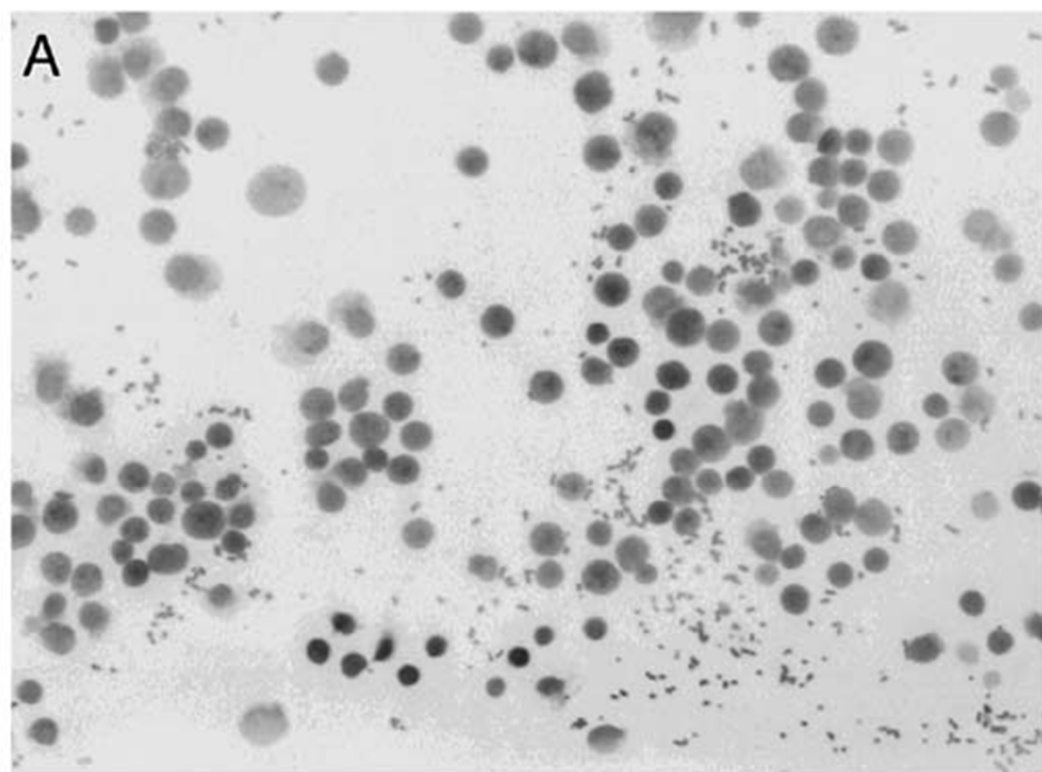


# *Routine Samples for Hematological Malignancies*

- *1. Bone Marrow is the standard choice for bone marrow cytogenetics analysis (1 cc of bone marrow in sodium heparin tube is required).*
- *2. Leukemic blood samples may be sent in cases where BM is difficult to obtain (5-10 cc blood in a sodium heparin tube)*
- *3. For CLL, the choice of sample is peripheral blood, however BM may also be sent.*

# HCMC CYTOGENETICS LABORATORY







**Human male  
G-bands**

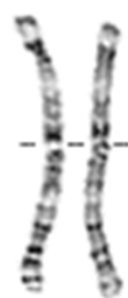




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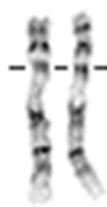
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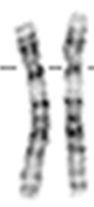
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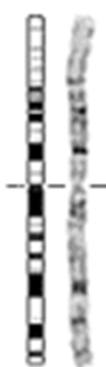
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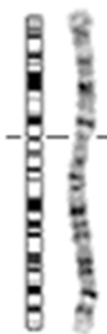
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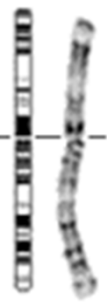
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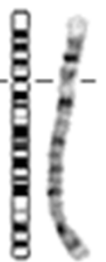
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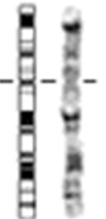
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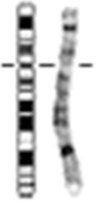
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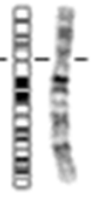
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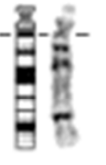
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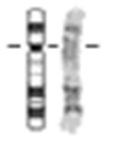
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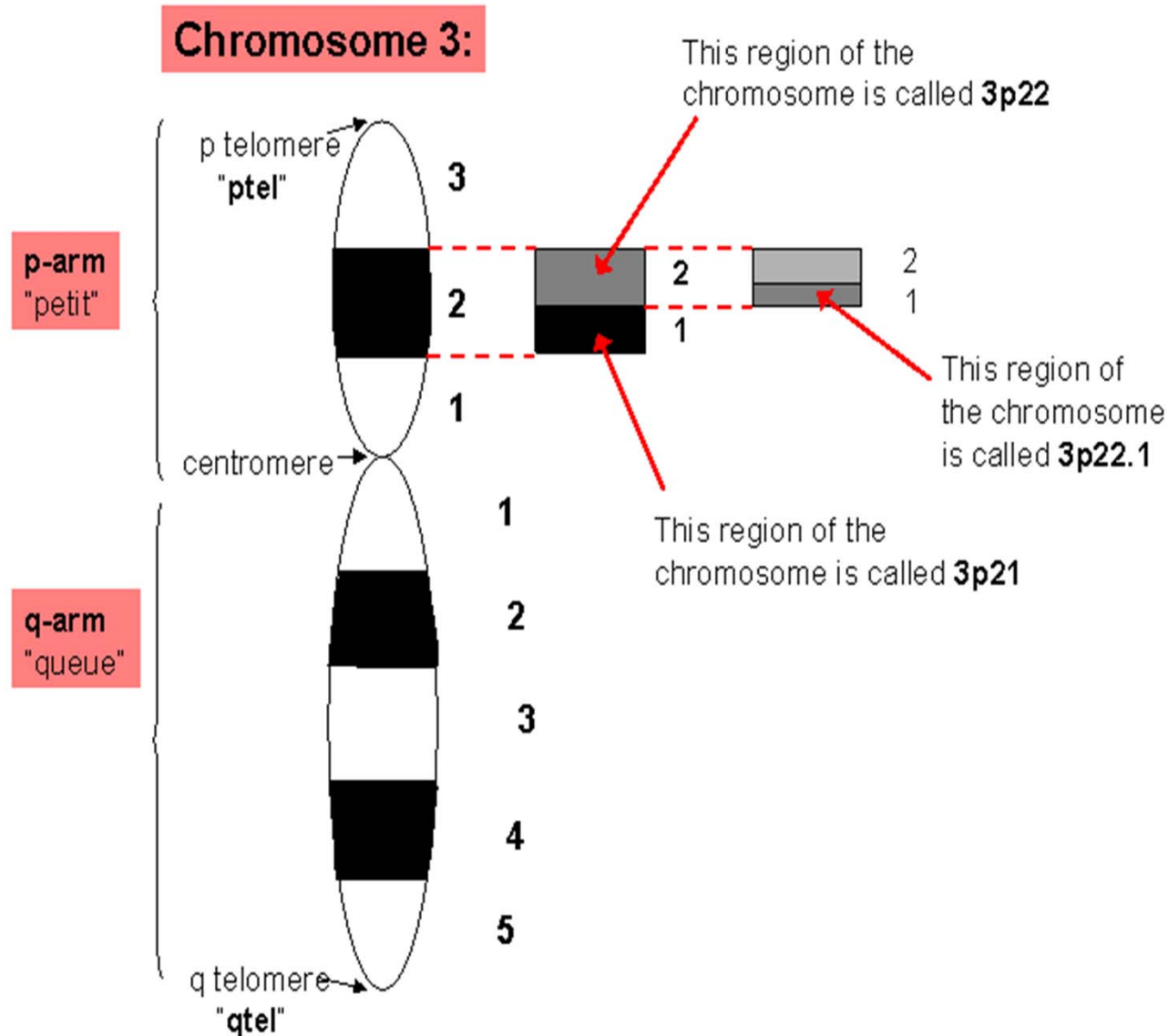
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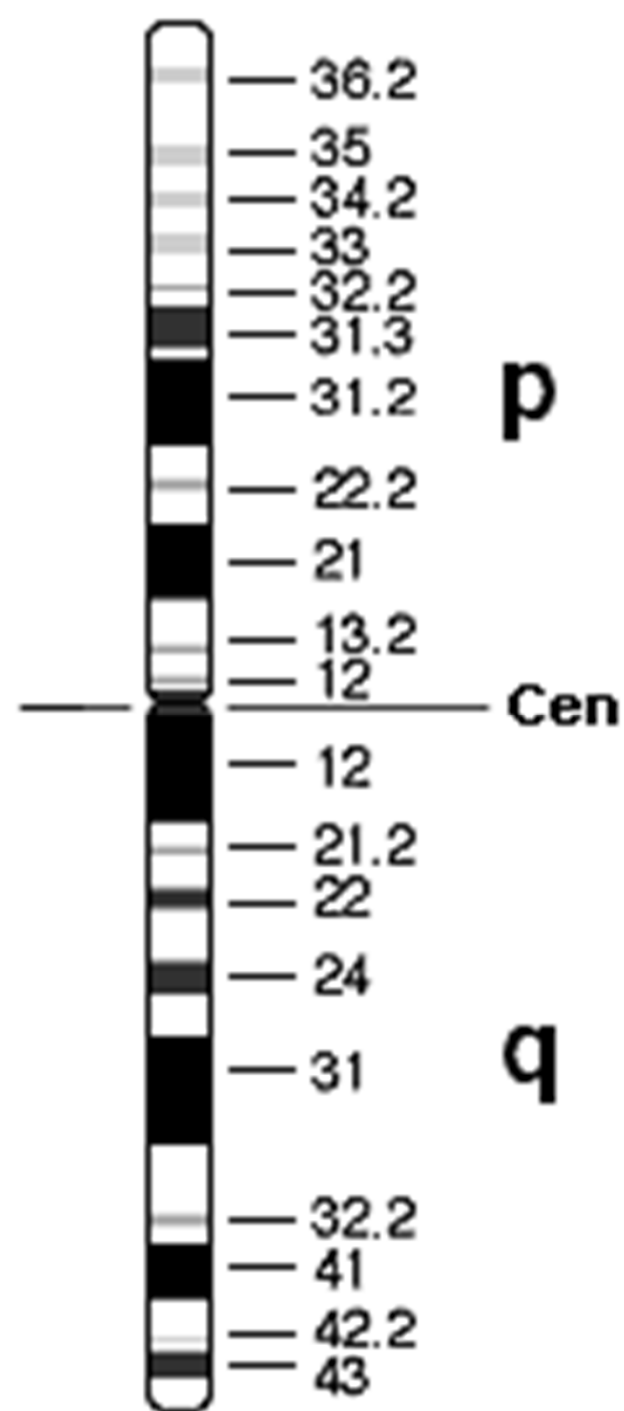


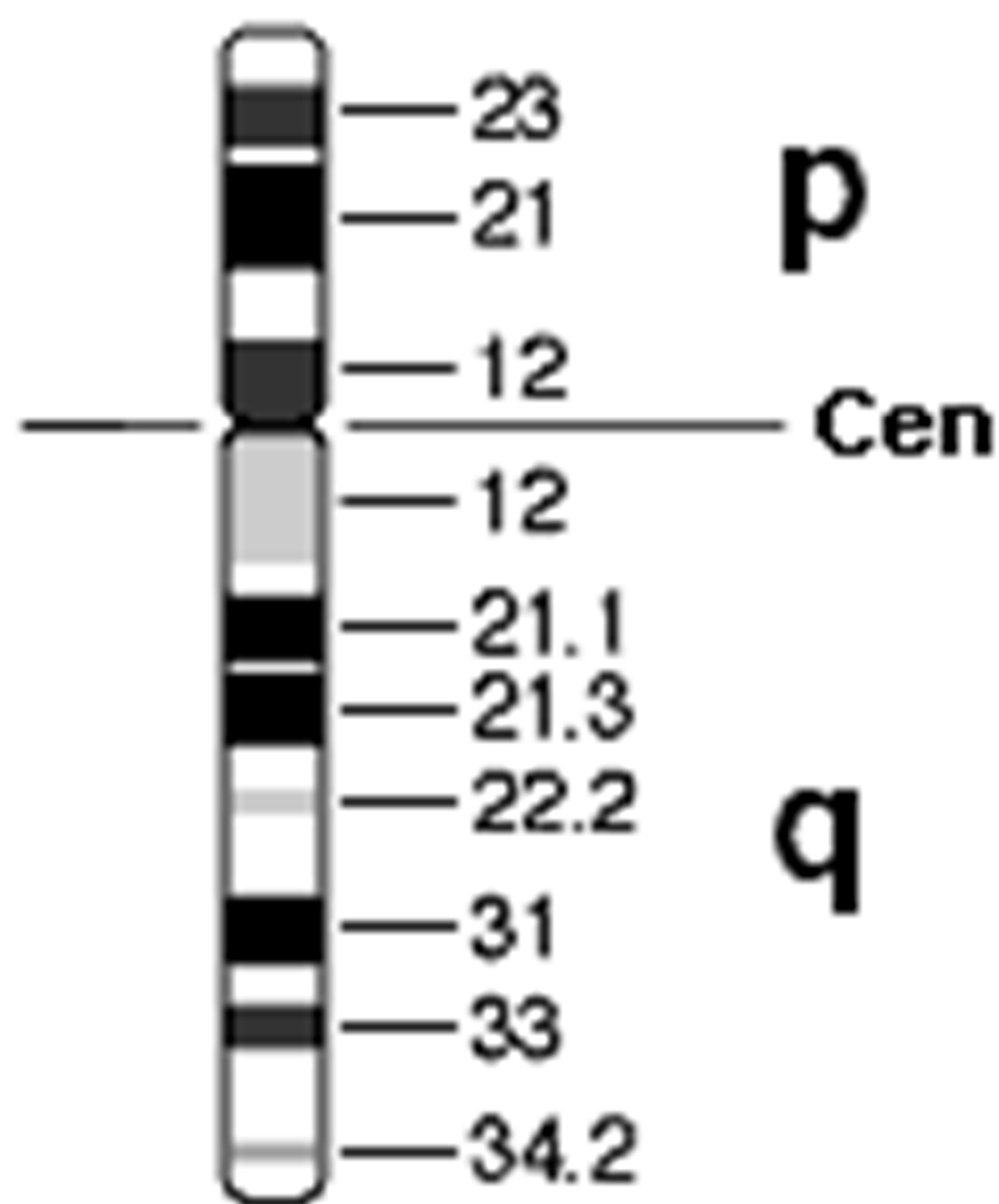
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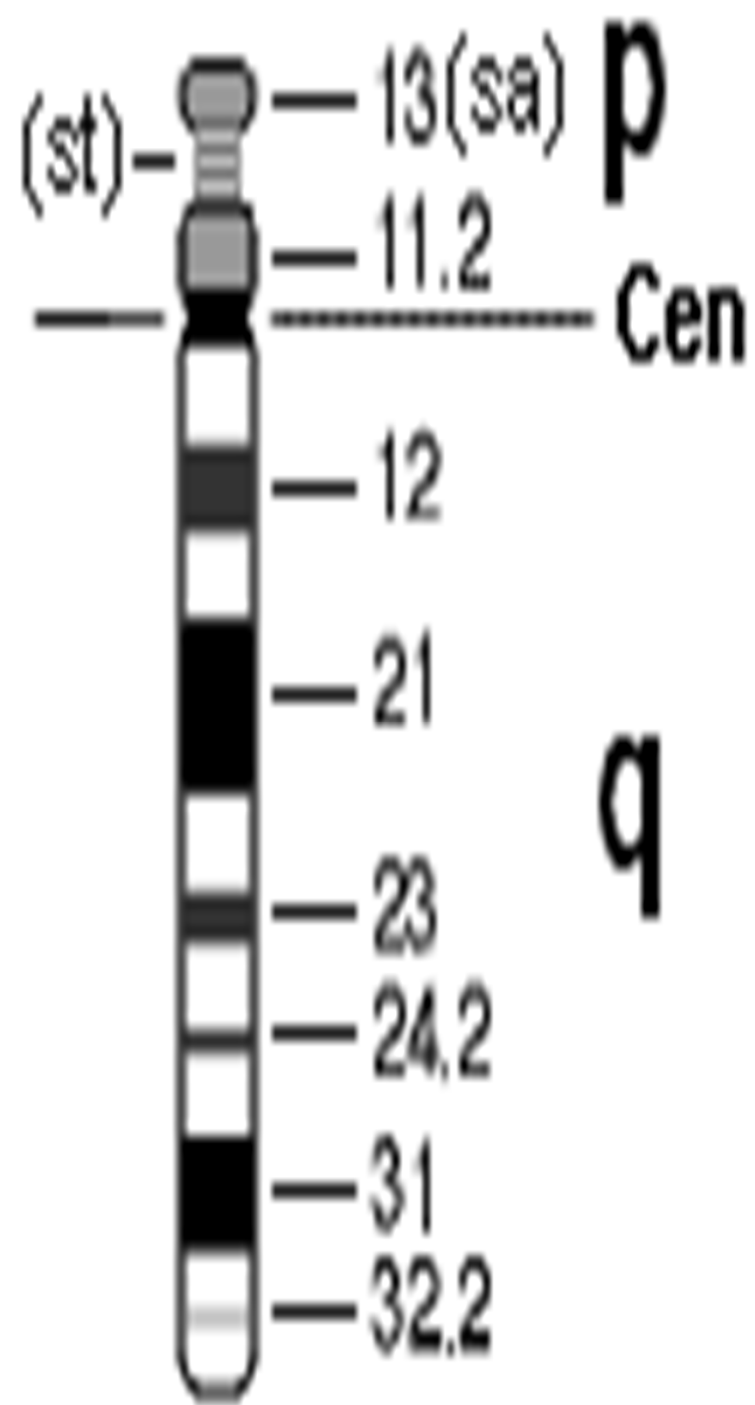
# Cytogenetic Banding Nomenclature











## ***Animated Inversion***

***Animated Translocation***





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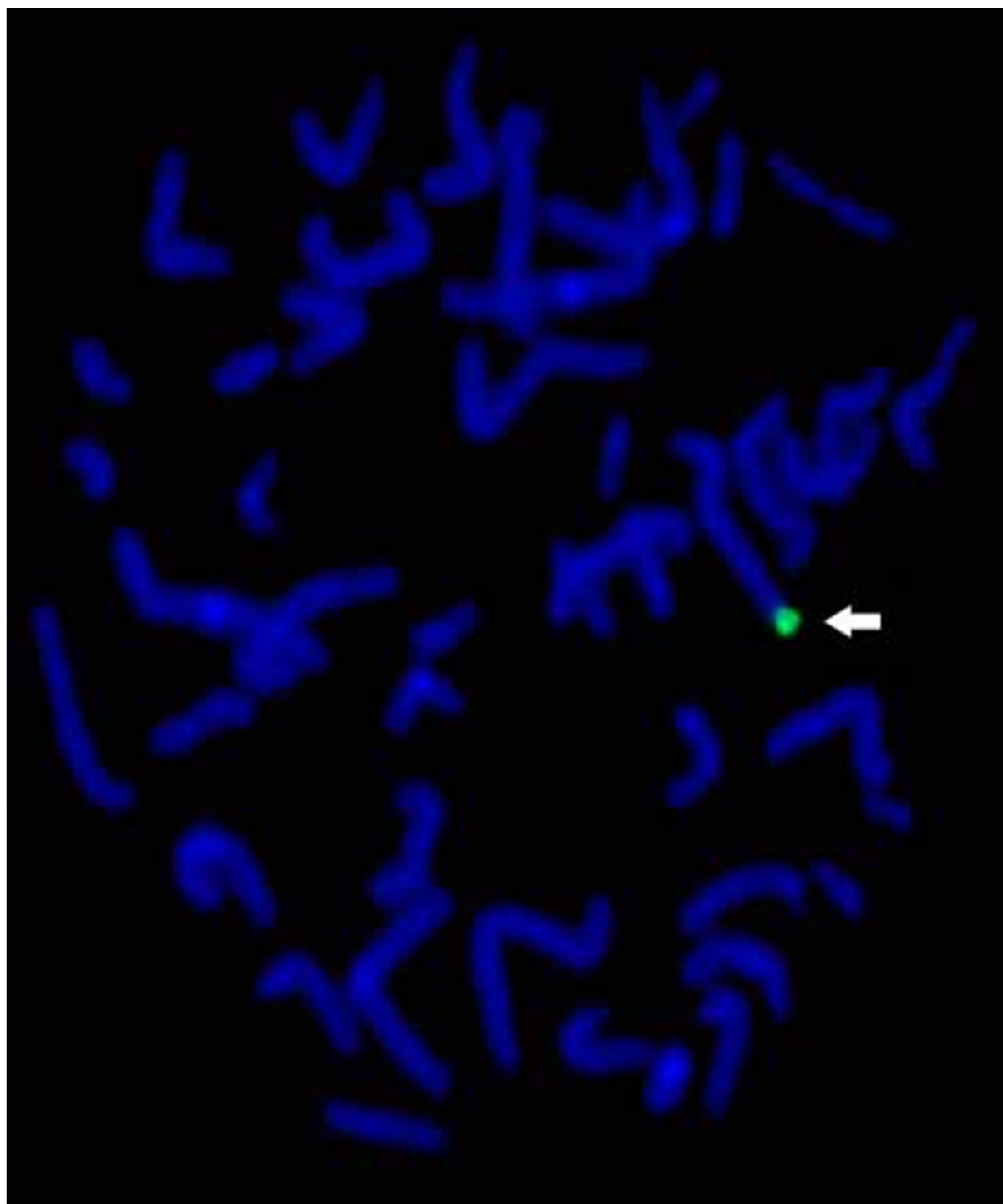
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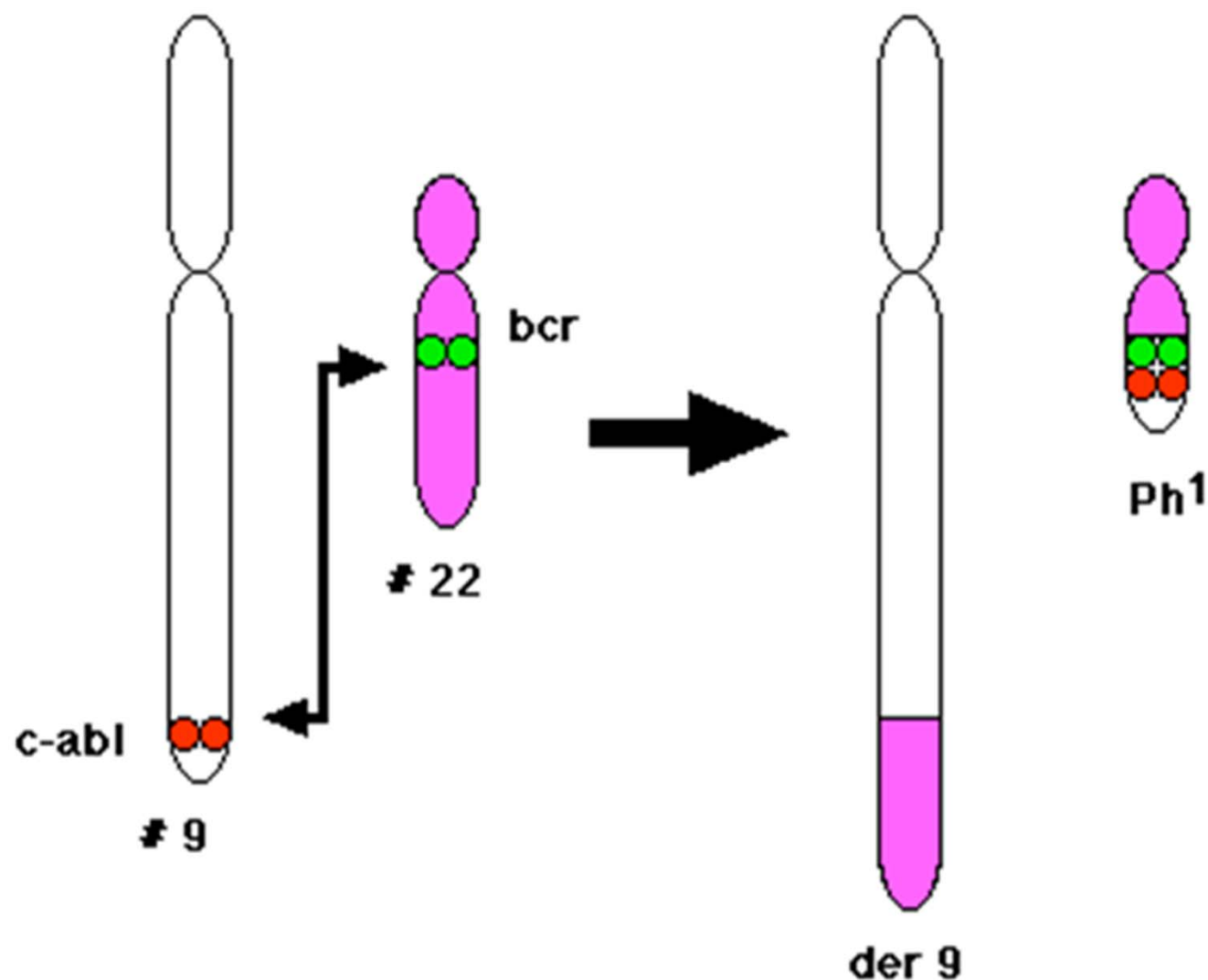


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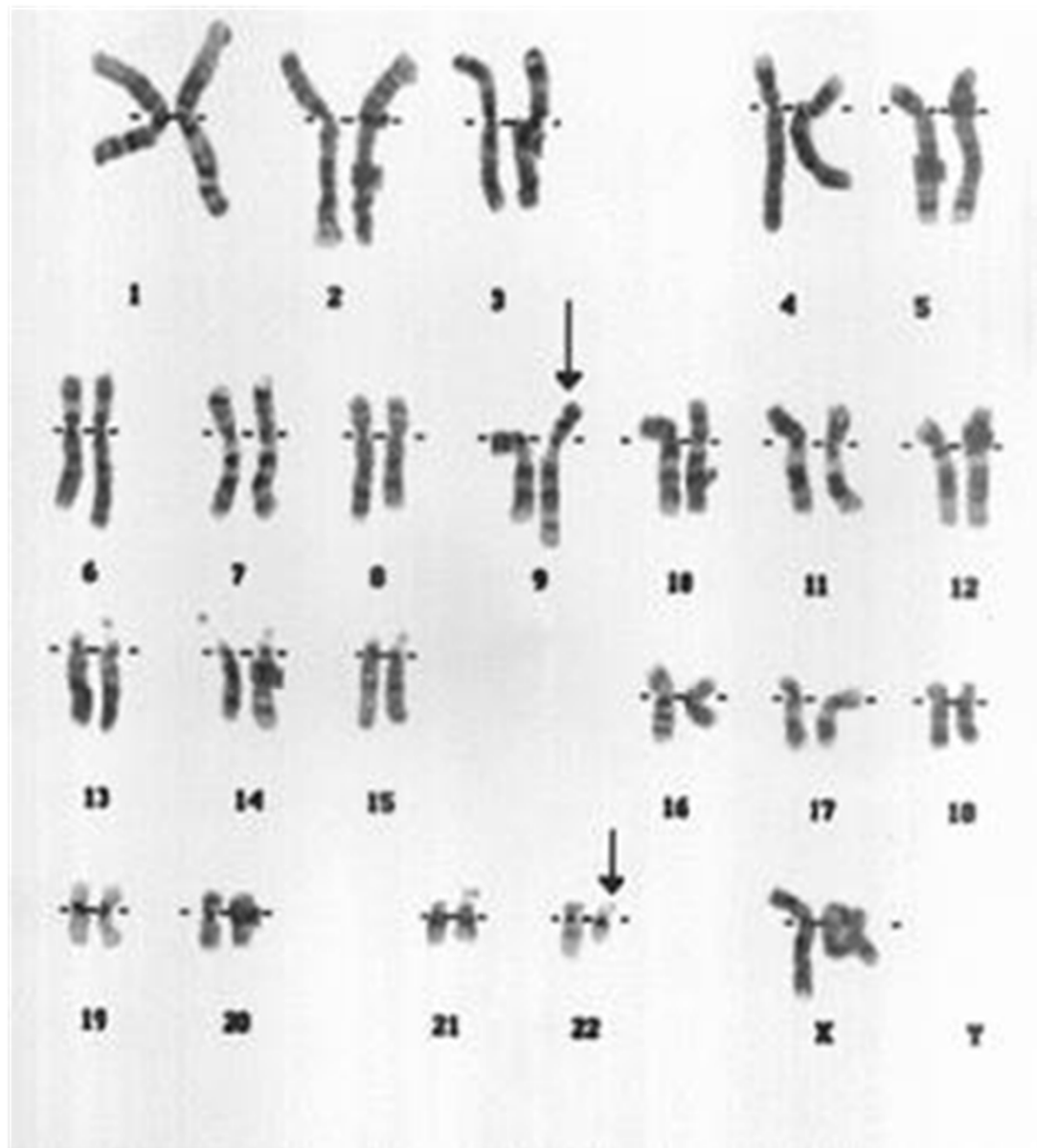
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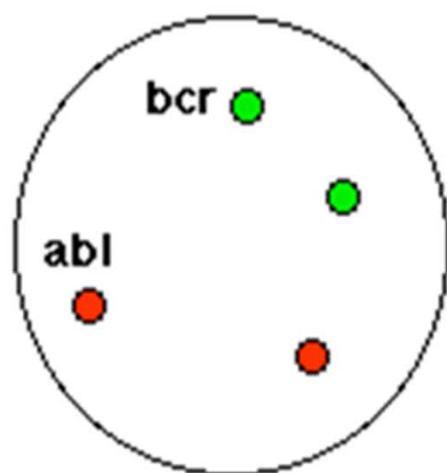
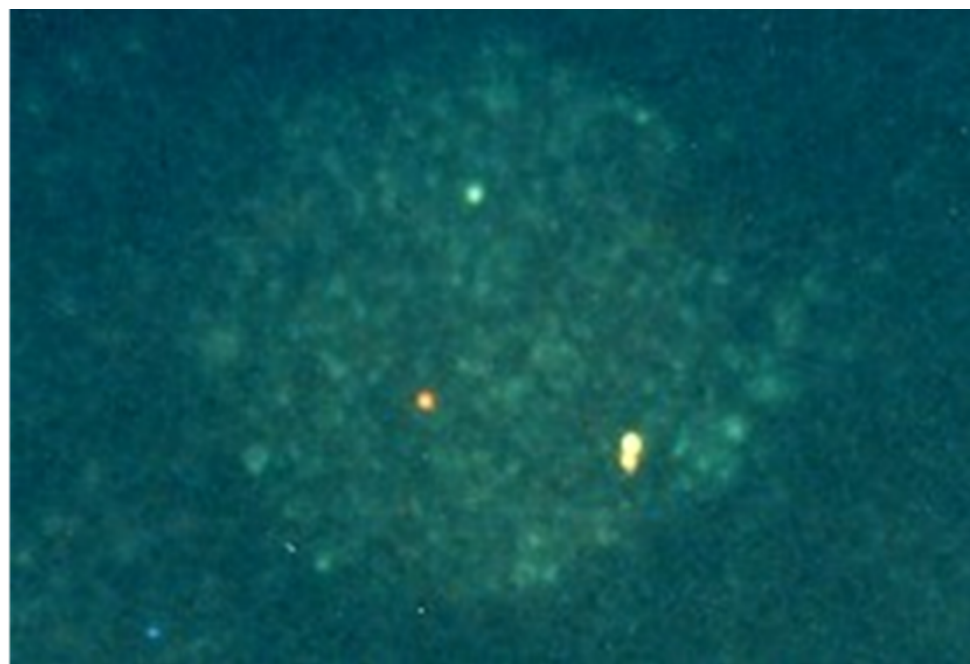


Reciprocal translocation between one # 9 and one #22 chromosome forms an extra-long chromosome 9 ("der 9") and the Philadelphia chromosome (Ph<sup>1</sup>) containing the fused abl-bcr gene. This is a schematic view representing metaphase chromosomes.

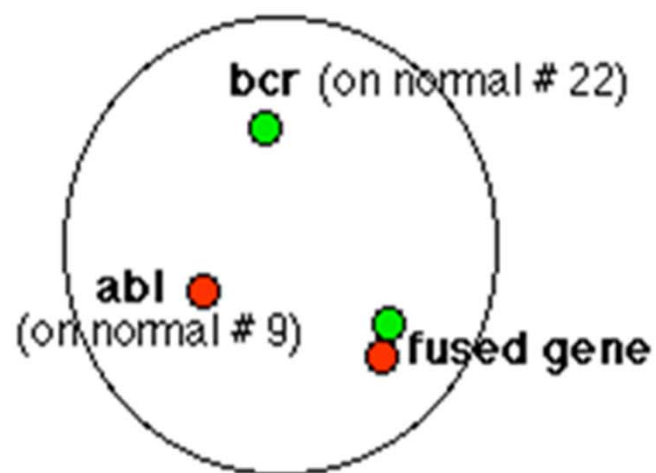




The abnormality seen by Nowell & Hungerford on chromosome 22, Now known as the Philadelphia Chromosome.



Normal interphase nucleus



Interphase nucleus of  
leukemic cell containing  
the Philadelphia  
chromosome (Ph<sup>1</sup>)

# *Chromosomal Abnormalities*

- Numerical:

Normal human somatic cells have 46 chromosomes called Diploid number (22 pairs of homologs of autosomes and two sex chromosomes. 46,XX or 46,XY

Monosomy: Loss of one chromosome (-7)

Trisomy: Gain of an extra chromosome(+8)

Hyperdiploidy: Gain of several chromosomes

Hypodiploidy: Loss of several chromosomes

## *Structural Chromosomal Aberrations*

- Consider a **normal** chromosome with genes in alphabetical order: abcdefghi
- --**deletion**: part of the chromosome has been removed: abcghi
- --**inversion**: part of the chromosome has been re-inserted in reverse order: abcfedghi
- --**ring**: the ends of the chromosome are joined together to make a ring
- --**translocation**: parts of two non-homologous chromosomes are joined: if one normal chromosome is abcdefghi and the other chromosome is uvwxyz, then a translocation between them would be abcdefxyz and uvwghi.



# *Cytogenetics in Hematological Disorders*

*Cytogenetic data is currently evaluated for diagnosis in:*

*Most of Myeloid Neoplasms to include AML,  
MDS and Chronic MPDs e.g. CML.*

*Specific cytogenetic abnormalities also characterize  
Lymphoid Disorders like Burkitt Lymphoma*

*Characteristic Chromosomal Breakages are associated  
with Fanconi's Anemia*

# *Cytogenetics in Hematological Neoplasms*

*Prognostic Significance: Varied Intensities of Therapy*

*Philadelphia chromosome positivity in ALL*

*Hyperdiploidy/ Hypodiploidy in ALL*

*MDS      Monosomy 7 or del(7q)  
del(5q)*



# *Cytogenetics in Chronic Myeloproliferative Disorders*

- Philadelphia Chromosome  
t(9;22)(q34;q11)(BCR/ABL)translocation
- Differentiates CML from other MPDs  
(ET,PV,CIMF,CNL,CEL) and MDS / MPD  
Diseases (CMML, a CML, JMML)

# *Cytogenetic Evolution in CML Blast Crisis*

$+Ph$

$i(17q)$

$+8$

$+19$

## *Acute Myeloid Leukemias with Recurrent Cytogenetic Abnormalities*

- AML with t(8;21)(q22;q22),(AML1/ETO) (FAB M2)
- AML with Abnormal Eosinophils (FAB M4Eo) inv(16)(p13q22) or t(16;16)(p13;q22),(CBF $\beta$ /MYH11)
- Acute Promyelocytic Leukemia (AML with t(15;17)(q22;q21),(PML/RAR $\alpha$ ) (FAB M3)
- AML with 11q23(MLL) abnormalities



# *Monitoring of Disease*

- Complete Cytogenetic Remission
- Relapse
- Evolution to an aggressive phase
- Secondary Cytogenetic changes due to therapy



**THANK YOU**